CBER Update: Challenges, Accomplishments, Initiatives

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CBER: The Reality

- CBER touches people's lives every day
- The job of protecting consumers remains a daily challenge
- The job is growing in scope and complexity
- Goal: protecting and advancing the public health through innovation

Vision for CBER

INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

- Protect and improve public and individual health in the US and, when feasible, globally
- Facilitate the development, approval, and access to safe and effective products and promising new technologies
- Strengthen CBER as a preeminent regulatory organization for biologics

Products Regulated by CBER

- Blood, blood components and derivatives
- Vaccines (preventive and therapeutic)
- Allergenics
- Cell and gene therapies
- Tissues
- Xenotransplantation
- Related devices

Personnel Update

- OCTGT
  - Dr. Celia Witten – Director
  - Dr. Joyce Frey – Deputy
- OCBQ
  - Mary Malarkey – Director
- OVRR
  - Dr.Norman Baylor – Acting Director
- OBRR
  - Dr. Jonathan Goldsmith - Deputy
- OBE
  - Dr. Mary Foulkes – Acting Director

CBER Touches the Lives of People Every Day

- 14 million units of blood and blood components are transfused yearly in U.S.
- More than 235 million vaccinations given each year to prevent serious infectious diseases
- 1 million tissues (e.g., bone, skin, ligaments) were transplanted last year to repair injury, restore function, and improve quality of life
- 800 active human trials studying experimental cell, gene, vaccine, or blood products for serious diseases, e.g., HIV, Cancer, Diabetes, Heart Disease

Challenges/Accomplishments Counterterrorism

- Need for safe and effective products to respond to terrorism
- Now ~ 25% of CBER effort/resource use
- Emergency availability of critical countermeasures for smallpox, botulinum and anthrax threats; EUA for anthrax vaccine issued
- Critical participation in multiple Task Forces including industry, CDC, NIH and DOD to facilitate product development
- Implementation of Project BioShield

Challenges/Accomplishments Patient Safety

- Patient Safety Efforts
  - Joint CBER/CDER guidances
    - Risk assessment, management, and pharmacovigilance
  - Joint CBER/CDER/CDRH guidance
    - Data monitoring committees
  - Collaboration with CMS on vaccine safety
  - VAERS data-mining projects

Challenges/Accomplishments International Efforts

- Advancing public health- an international challenge; we are a critical player
- New MOUs: EU, Canada, Switzerland
- Xenotransplantation, tissues and gene therapy outreach with WHO, others
- ICH (including Gene Therapies)
- GHTF (devices)
- Pharmaceutical Inspection Cooperation Scheme (PIC/S)
- ICDRA

Challenges/Accomplishments Vaccine Safety

- Vaccine Safety Efforts
  - Thimerosal eliminated or reduced to trace amounts in all childhood vaccines, except some flu vaccines
  - Improve detection of possible vaccine adverse events
  - Enhanced adverse event reporting and safety monitoring using VAERS, CDC Vaccine Safety Datalink, and advanced data mining

Challenges/Accomplishments Vaccine Safety (continued)

- Vaccine to protect children against *Streptococcus pneumoniae* infection
  - infection causes 200 deaths, 700 cases of meningitis, 17,000 cases of blood infection, and almost 5 million cases of ear infections each year
  - Approved Prevnar, a vaccine that prevents *S. pnemoniae* infection

Challenges/Accomplishments
Flu Vaccine

- **Flu Vaccine – Facilitate an adequate and safe supply of annual flu vaccine and preparedness for an influenza pandemic**
  - **Rapidly facilitated use of unlicensed vaccine for 2004-2005 under appropriate regulatory guidelines to address vaccine shortage**
  - **Working intensively with Chiron to resolve production problems for 2005-2006**
  - **Accelerated approval mechanism using surrogate markers**
  - **Helping additional manufacturers attain US licensure, increasing capacity**

Challenges/Accomplishments Blood Safety

- Continuous need to protect blood from infectious agents, e.g., HIV, hepatitis, West Nile, vCJD
  - Investigational West Nile assay rapidly developed within less than 8 months to screen entire U.S. blood supply; over 1,000 infected units intercepted before transfusion
  - Steps to reduce vCJD risk taken even before transfusion transmission documented
  - NAT testing to shorten window period (HIV, HCV)

Challenges/Accomplishments Blood Safety (continued)

- HIV – need to better detect infection to inform patients, allow treatment, and improve public health interventions
  - CDC estimates that nearly 250,000 HIV infected people in the U.S. are not aware they are infected
  - OraQuick Rapid oral fluid test approved expanding field testing for at-risk populations globally

Challenges/Accomplishments Blood Safety (continued)

Blood Substitutes – Need safe and effective alternatives to human blood, to respond to increased demand for blood, needs in remote areas, military, and terrorism situations, risks of infectious disease transmission, and short product shelf life

- **Accomplishment:**
  - **FDA research on toxicity of synthetic red cell substitutes helps manufacturers better predict and prevent toxicity**

Challenges/Accomplishments Tissue Safety

More than 1 million tissues transplanted yearly, e.g., bone, skin, ligaments transplanted each year; safety concerns remain a top priority

- Accomplishment:
  - Comprehensive risk-based regulatory framework for tissues put in place to ensure donor suitability and proper tissue collection, processing, and handling and reduce the risk of infectious diseases

  - Tissue Safety Team –cross-cutting
    - Develop SOPs to facilitate AEs
    - Shared databases
    - Liaison with ORA, CDC, HRSA

Challenges/Accomplishments Gene and Cellular Therapies

- Gene and stem cell therapies – Protect patients enrolled in clinical trials from serious adverse effects while allowing development of and access to promising new therapies

- Accomplishments:
  - GeMCRIS database launched in collaboration with NIH to collect, analyze and share adverse event data
  - Development of toxicity models and criteria for long-term patient follow up for adverse events
  - Standards produced to assure consistent and safe dosing of gene therapy vectors (e.g. adenovirus)

Challenges/Accomplishments Review Management

- Complex products, ever tightening budget, statutory deadlines
- Accomplishments:
- Combination Products processes/guidance
- PDUFA and MDUFMA
  - Meeting goals
  - Modular reviews
  - Interactions with Stakeholders
  - Work closely with CDER, CDRH
  - Collaborative reviews

Challenges/Accomplishments Critical Path

Products more complex, need better scientific tools to evaluate product safety and efficacy

- Accomplishments:
  - Facilitating development of methods to detect and inactivate new infectious agents to ensure biologic product safety
  - Development of better assays, standards, biomarkers and animal models to define product potency, purity and effectiveness

Partnerships

- The NCI-FDA Research and Regulatory Review Fellowship program trains a cadre of researchers to bridge the processes from scientific discovery through clinical development and regulatory review of new oncology products
- CBER-CDC-Industry – Development of diagnostic tests and standards to screen blood donors for West Nile Virus
- CBER-Plasma Industry – Technical standards for plasma-derived products

Partnerships

- CBER-AABB-Blood Industry disaster task force to respond to disasters and BT events
- CBER-WHO – Development of global vaccine and thrombin standards
- CBER-CDC-NIH-HHS-WHO Pandemic Flu – Supporting vaccine development to respond to potential avian flu pandemic
- CBER-CMS – Review data from CMS health systems database for vaccine problems
- CBER-CDC-NIH – Supporting development of SARS vaccine

CBER Initiatives

- Management and Organizational Initiatives
  - FDA's Gallup Program Survey- opportunity for feedback and improvement
  - Human Capital Development
    - Management development
    - Succession planning
    - Enhance training opportunities
    - Continue to recruit, build and support a strong team

CBER Initiatives

- Advance development of biologics
  - Critical path
  - Review management enhancements
    - Training, templates
  - Guidance
  - Stakeholder communications/meetings

CBER Initiatives

- Use of Expert Consultants
- Develop CBER-CDRH pilot – combination product review processes
- Lot release testing and lab quality programs
- Develop global health priorities

Thank you!

- Exciting future – working together
- Lots of challenges/opportunities
- Contact us: matt@cber.fda.gov
- We welcome your input!